ANALYSIS OF ESTIMATORS FOR ADAPTIVE KINETIC MONTE CARLO

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Abstract. Adaptive Kinetic Monte Carlo combines the simplicity of Kinetic Monte Carlo (KMC) with a Molecular Dynamics (MD) based saddle point search algorithm in order to simulate metastable systems. Key to making Adaptive KMC effective is a stopping criterion for the saddle point search. In this work, we examine a criterion, recently appearing in [6], that is based on the fraction of total reaction rate found instead of the fraction of observed saddles. The criterion uses the Eyring-Kramers law to estimate the reaction rate at the MD search temperature. We also consider a related criterion that remains valid when the Eyring-Kramers law is not. We examine the mathematical properties of both estimators and prove their mean square errors are well behaved, vanishing as the simulation continues to run.

1. Introduction

An outstanding problem in theoretical materials science and chemistry is how to reach laboratory time scales of microseconds (10^{-6} s) and longer using Molecular Dynamics (MD) based models which resolve the atomistic time scale of femtoseconds (10^{-15} s). Much of this scale separation is due to the presence of *metastable* regions in the configuration space of the system. In such regions, often defined by local minima of an energy landscape, the system stays close to a particular configuration, such as a local minima, before crossing into some other metastable region associated with a different configuration. Consequently, during much of a direct MD simulation, the system is close to one metastable region or another. It exhibits dynamics akin to a continuous time random walk on the set of metastable states, with comparatively long waiting times.

Since much of the physical significance of these systems is characterized by the sequence of visited metastable states and the time spent in each, there have been a variety of efforts to systematically coarse grain the MD trajectory into a more computationally efficient continuous time random walk. A.F. Voter has proposed three methods, Parallel Replica Dynamics, Hyperdynamics, and Temperature Accelerated Dynamics, which can overcome metastability through intelligent usage of the primitive Langevin dynamics, [14, 16]. In recent years, significant effort has been made to understand and quantify the approximations in these methods and extend their applicability, [1–3, 5, 11, 12, 15].

Another approach to the problem is Kinetic Monte Carlo (KMC), and this will be the focus of this work. Let us assume our system is governed by a potential energy $V(x)$, $x \in \mathbb{R}^d$ at inverse temperature β. Furthermore, we assume that we have

partitioned configuration space into an at most countable set of metastable states, Ω_i, associated with local minima m_i of V. The system can go from metastable state i to metastable state j if there is a saddle point, s_{ij}, of $V(x)$ joining Ω_i and Ω_j. For conciseness, we will assume there is a single saddle point joining two given adjacent metastable states, though, in general, there may be multiple pathways.

In traditional KMC, before a simulation is run, one must identify the metastable states, their connectivity (*i.e.*, which ones are joined by saddle points), and the reaction rates of each such connection. Given all of this information, KMC is very cheap to simulate. A single random number is generated and used to select one of the possible reactions, the system migrates into the new metastable region, and the algorithm repeats.

Unfortunately, such complete details of the metastable states and their connectivity are, *a priori*, unavailable in all but the simplest low dimensional systems. This has motivated the development of Adaptive Kinetic Monte Carlo (AKMC), [6, 17, 18]. In AKMC, the system starts in some metastable region Ω_i. Saddle points associated with Ω_i are then sought via a *saddle point search algorithm* that successively finds s_{ij}. Reaction rates for each such saddle can be estimated by the Eyring-Kramers law [8]:

$$(1.1) \qquad k_{ij} = g_{ij} \exp\left[-\beta(V(s_{ij}) - V(m_i))\right],$$

where, writing λ_1 for the sole negative eigenvalue of $\nabla^2 V(s_{ij})$,

$$g_{ij} = \frac{|\lambda_1|}{\pi} \sqrt{\left|\frac{\det\nabla^2 V(m_i)}{\det\nabla^2 V(s_{ij})}\right|}.$$

Once a sufficient number of saddles associated with Ω_i have been identified, the problem is treated by using traditional KMC with the thus far identified reactions and their rates; this process then repeats in the next metastable region. Two things are needed to proceed with AKMC:

(1) A saddle point search algorithm;
(2) A stopping criterion.

In this work, we will consider the question of the stopping criterion, provided our saddle point search algorithm satisfies certain assumptions. Our analysis will focus on estimators similar to the one introduced by Chill & Henkelman in [6]. We call these *Chill type estimators*.

In [6], the authors searched for saddle points out of each metastable state using high temperature MD. For concreteness, consider the Brownian dynamics in $\mathbb{R}^d$:

$$(1.2) \qquad dX_t = -\nabla V(X_t)dt + \sqrt{2\beta^{-1}}dW_t.$$

The aim is to model the dynamics at low temperature $\beta = \beta^{\mathrm{lo}}$. Starting at $X_0 \in \Omega_i$, integrate (1.2) at a higher temperature $\beta = \beta^{\mathrm{hi}}$ (*i.e.*, $\beta^{\mathrm{lo}} > \beta^{\mathrm{hi}}$) until the trajectory leaves Ω_i. Using the higher temperature β^{hi} allows an escape to occur more quickly. After the trajectory leaves Ω_i, one of the saddle points s_{ij} is identified with this pathway using, for instance, the nudged elastic band method [9, 10], and the low temperature reaction rate is computed using (1.1) with $\beta = \beta^{\mathrm{lo}}$. This is then repeated, with a new initial condition chosen in Ω_i. Throughout, the cumulative simulation time is recorded.

Other saddle point search algorithms have been proposed, including the Dimer method and the string method [7, 13]. In our analysis, the key property that we

need to hold true for all of our search methods is the following. Let

(1.3) $N_{ij}(t) = $ Number of times saddle s_{ij} has been found by time t.

Then for fixed i, during a saddle point search, the $N_{ij}(t)$ are independent, with respect to j, Poisson processes. We prove below that this holds for a carefully performed saddle point search via integration of (1.2).

This article is organized as follows. We describe the saddle point search in detail in Section 2 below, and prove some of its properties, including the above condition on $N_{ij}(t)$, in Section 3 below. In Section 4 we introduce stopping criteria for the saddle point search, and in Section 5 we analyze these criteria. Section 6 contains proofs of some of the estimates in Section 5. In Section 7 we make some concluding remarks.

2. Notation and saddle point search algorithm

Here and throughout (X_t) is Brownian dynamics, that is, a stochastic process satisfying (1.2). For simplicity we fix a single metastable set $\Omega \equiv \Omega_i$ and suppress the index i in all of our notations from the Introduction. For our purposes, V is smooth, and Ω is an (open) basin of attraction of V with respect to the gradient dynamics $dy/dt = -\nabla V(y)$. We assume that $\partial\Omega$ is partitioned into finitely many disjoint (measurable) subsets, called *pathways* and labeled $1, 2, \ldots, N$, such that each pathway j contains a unique saddle point s_j of V. When (X_t) leaves Ω, it must exit through one of the pathways $1, 2, \ldots, N$.

The algorithm, as well as our analysis, depends heavily on the quasistationary distribution (QSD) for (X_t) in Ω, which we denote by ν. The QSD ν is a probability measure that is locally invariant for (X_t), in the sense that it is invariant conditionally on the event that (X_t) remains in Ω:

Definition 2.1. *The QSD for (X_t) in Ω is a probability measure ν supported in Ω such that for all $t > 0$,*

$$\nu(\cdot) = \mathbb{P}(X_t \in \cdot \mid X_0 \sim \nu, \, X_s \in \Omega \text{ for all } s \in [0, t]).$$

Of course ν depends on Ω, but for simplicity we do not indicate this explicitly. It has been shown [11] that ν exists, is unique, and satisfies

(2.1) $\nu(A) = \lim_{n \to \infty} \mathbb{P}(X_t \in A \mid X_s \in A \text{ for } s \in [0, t]), \qquad \text{for all } A \subset \Omega.$

Moreover this convergence is exponentially fast, uniformly in A. Equation (2.1) leads to simple algorithms for sampling ν, based on the idea that a sample can be obtained from the endpoint of a trajectory of (X_t) that has remained in Ω for a sufficiently long time; see [5] for details.

We are now ready to state the high temperature saddle point search algorithm. Versions of this algorithm have been used previously; see for instance [6] and references therein. The search runs at a user-specified "high" (inverse) temperature β^{hi}. Below we write ν for the QSD in Ω at temperature $\beta = \beta^{\text{hi}}$. We also write

$$H(t) = \begin{cases} 0, & t < 0 \\ 1, & t \geq 0 \end{cases}$$

for the Heaviside unit step function.

Algorithm 2.2. *Set $N_j(t) \equiv 0$ for $t \geq 0$ and $j = 1, \ldots, N$. Let M be the current cycle of the algorithm, and t_{sim} the simulation clock. Initialize $M = 1$ and $t_{\mathrm{sim}} = 0$, and iterate the following:*

1. *Generate a sample x_M from ν. The simulation clock t_{sim} is stopped during this step.*
2. *Starting at $X_0 = x_M$, evolve (X_t) at $\beta = \beta^{\mathrm{hi}}$ until it first leaves Ω, say at time $t = \tau^{(M)}$ through pathway $I^{(M)}$. The simulation clock t_{sim} is running during this step, and the stopping criterion is continuously checked. If at some time t_{sim} the criterion is met, the algorithm stops.*
3. *If $I^{(M)} = j$, update $N_j(t) = N_j(t) + H(t - t_{\mathrm{sim}})$ for $t \geq 0$ and record the saddle point s_j. Then update $M = M + 1$. The simulation clock t_{sim} is stopped during this step.*

It is not necessary to know N, and the pathways can be given labels according to the order in which they are found. The simulation clock is cumulative, and it only increases in Step 2. In particular, during the M-th cycle of the algorithm, t_{sim} increases by $\tau^{(M)}$. The stopping criterion will be described in Section 4. Below we write t_{sim} for the final value of the simulation clock in the algorithm, that is, its value when the simulation is stopped. To refer to a generic simulation clock time we write t. Thus, $0 \leq t \leq t_{\mathrm{sim}}$ and when the algorithm stops, $N_j(t)$ is the number of times an exit through pathway j has been observed by time t. Below we write $N_j(t)$ for its final value when the algorithm stops. We will also use the following notations:

$$(2.2) \qquad \chi_j(t) = \mathbb{1}_{N_j(t) \geq 1}, \qquad N(t) = \sum_{j=1}^{N} N_j(t).$$

That is, $\chi_j(t) = 1$ if an exit through pathway j has been observed at least once by time t, and is 0 otherwise; $N(t)$ is the total number of exits observed by time t.

3. Properties of the saddle point search

Our first result follows immediately from properties of the QSD established in [11].

Theorem 3.1. *Suppose that in Step 1 in the M-th cycle of Algorithm 2.2, x_M is a random variable with distribution ν. Then:*

(i) *$\tau^{(M)}$ is exponentially distributed with mean κ^{-1}: $\mathbb{P}(\tau^{(j)} > t) = \exp(-\kappa t)$,*
(ii) *$\tau^{(M)}$ and $I^{(M)}$ are independent.*

Theorem 3.1 then leads to the following.

Theorem 3.2. *Suppose that in Step 1 of Algorithm 2.2, $x_1, x_2, \ldots$ are iid with common distribution ν. Then:*

(i) *$\{N(t)\}_{0 \leq t \leq t_{\mathrm{sim}}}$ is a Poisson process with parameter κ,*

(ii) *$\{N_j(t)\}_{0 \leq t \leq t_{\mathrm{sim}}}^{j=1,\ldots,N}$, are independent Poisson processes with parameters*

$$(3.1) \qquad \kappa_j := \kappa\, p_j, \qquad p_j := \mathbb{P}(I^{(1)} = j).$$

Proof. Let $(\tilde{N}(s))_{s \geq 0}$ be a Poisson process with parameter κ, which we denote by $\tilde{N}(s)$ for brevity. Label each arrival time of $\tilde{N}(s)$ with a pathway j according to

the distribution p_j, independently of the other arrival times, and let $\tilde{N}_j(s)$ be the process with arrivals labeled by j. Then for $r, s \geq 0$ and $m_1, \ldots, m_N \geq 0$,

$$\mathbb{P}\left(\bigcap_{j=1}^{N}\left\{\tilde{N}_j(r+s) - \tilde{N}_j(r) = m_j\right\}\right)$$

$$(3.2) \qquad = \mathbb{P}\left(N(r+s) - N(r) = \sum_{j=1}^{N} m_j\right)\binom{m_1 + \ldots + m_N}{m_1, \ldots, m_N}\prod_{j=1}^{N} p_j^{m_j}$$

$$= \prod_{j=1}^{N} \frac{e^{-\kappa p_j s}(\kappa p_j s)^{m_j}}{m_j!}.$$

By summing over all $m_i \geq 0$ for $i \neq j$ in the last expression above, we see that for fixed $r, s \geq 0$, the increment $\tilde{N}_j(r+s) - \tilde{N}_j(r)$ is Poisson distributed with mean $\kappa p_j s$. $\tilde{N}_j(s)$ also inherits independent increments from $\tilde{N}(s)$. This shows that $\tilde{N}_j(s)$ is a Poisson process with parameter $\kappa_j = \kappa p_j$. Moreover, (3.2) shows that $\tilde{N}_j(s)$, $j = 1, \ldots, N$, are independent.

Let us now relate $(\tilde{N}(s))_{s \geq 0}$ with $(N(s))_{0 \leq s \leq t_{\text{sim}}}$. For fixed $s \in [0, t_{\text{sim}}]$, the time marginal $N(s)$ is the largest m such that $\tau^{(1)} + \ldots + \tau^{(m)} \leq s$. Together with part *(i)* of Theorem 3.1, this shows that on $[0, t_{\text{sim}}]$, $(N(s))_{0 \leq s \leq t_{\text{sim}}}$ and $(\tilde{N}(s))_{s \geq 0}$ are Poisson processes with the same law. By part *(ii)* of Theorem 3.1, it follows that the multivariate processes $(N_j(s))_{0 \leq s \leq t_{sim}}^{j=1,\ldots,N}$ and $(\tilde{N}_j(s))_{0 \leq s \leq t_{sim}}^{j=1,\ldots,N}$ have the same law. This establishes the result. $\qquad \square$

4. Chill type estimators and stopping criteria

The purpose of the high temperature saddle point search (Algorithm 2.2) is to locate "enough" of the low-temperature rate corresponding to the metastable set Ω. More precisely, at a low temperature corresponding to $\beta = \beta^{\text{lo}}$, the first exit time of X_t from Ω is approximately exponentially distributed with mean $(k_1 + \ldots + k_N)^{-1}$, where $k_j = k_j^{\text{lo}}$ is given by the Eyring-Kramers law (1.1) at $\beta = \beta^{\text{lo}}$ (recall the subscript i has been suppressed). See [4] and references therein for rigorous results in this direction. The k_j's are then exponential rates associated with leaving Ω through pathway j at low temperature β^{lo}. The proportion of low temperature rate found by time t in Algorithm 2.2 is

$$(4.1) \qquad R(t) := \frac{\sum_{j=1}^{N} \chi_j(t)k_j}{\sum_{j=1}^{N} k_j}.$$

The expected value of $R(t)$ is

$$(4.2) \qquad \mathbb{E}[R(t)] = \bar{R}(t) := \frac{\sum_{j=1}^{N} p_j(t)k_j}{\sum_{j=1}^{N} k_j},$$

where

$$(4.3) \qquad p_j(t) := \mathbb{E}[\chi_j(t)] = 1 - \exp(-\kappa_j t).$$

Here κ_j is defined as in Theorem 3.2 at temperature $\beta = \beta^{\text{hi}}$. The idea behind Chill-type estimators is that when $R(t)$ is sufficiently close to 1, the high temperature saddle point search can stop. There are two obstacles to this idea.

The first is that, at any time during Algorithm 2.2, it is unlikley that all saddle points have been found. This problem is remedied by replacing k_j in (4.1) with $\chi_j(t)k_j$, which is computable once pathway j has been found during the simulation. The second obstacle is that an exact formula for $p_j(t) := \mathbb{E}[\chi_j(t)]$ will not be known in practice. Chill-type estimators overcome the latter obstacle by using one of the following approximations:

(4.4)

$$\tilde{p}_j(t) := 1 - \exp[-k_j^{hi}t], \qquad k_j^{\mathrm{hi}} \text{ given by the Eyring-Kramers law at } \beta = \beta^{\mathrm{hi}},$$

$$\hat{p}_j(t) := 1 - \exp[-\hat{N}_j(t)], \qquad \hat{N}_j(t) := \begin{cases} N_j(t), & N_j(t) \geq 2, \\ 0, & \text{else} \end{cases}.$$

We have used the superscript $^{\mathrm{hi}}$ to indicate that the rate in (4.4) is computed at temperature β^{hi} (whereas k_j is computed at low temperature β^{lo}). Also note that $\tilde{p}_j(t)$ is a physical estimate of $\mathbb{E}[\chi_j(t)]$ based on Eyring-Kramers, while $\hat{p}_j(t)$ is a (biased) Monte Carlo estimator. From (4.4) we obtain the following estimators for $R(t)$:

(4.5) $$\tilde{R}(t) := \frac{\sum_{j=1}^{N} \tilde{p}_j(t)\chi_j(t)k_j}{\sum_{j=1}^{N} \chi_j(t)k_j}, \qquad \hat{R}(t) := \frac{\sum_{j=1}^{N} \hat{p}_j(t)\chi_j(t)k_j}{\sum_{j=1}^{N} \chi_j(t)k_j}.$$

$R(t)$, $\tilde{R}(t)$, and $\hat{R}(t)$ are all random, while $\bar{R}(t)$ is deterministic. Both $\tilde{R}(t)$ and $\hat{R}(t)$ are explicitly computable at time t during the saddle point search. See [6] for further discussion of $\tilde{R}(t)$. To our knowledge $\hat{R}(t)$ has not appeared before in the literature. We emphasize that $\hat{R}(t)$ may be used at any temperature β^{hi}, while $\tilde{R}(t)$ is limited by the fact that it gives reasonable estimates of $R(t)$ only at (relatively low) temperatures where the Eyring-Kramers law holds.

After choosing $\tilde{R}(t)$ (resp. $\hat{R}(t)$) as the preferred estimator, the stopping criterion can now be defined as follows: for a user-specified parameter $\epsilon > 0$, stop Algorithm 2.2 in Step 3 if and only if

(4.6) $$\tilde{R}(t) > 1 - \epsilon \qquad (\text{resp. } \hat{R}(t) > 1 - \epsilon).$$

In Section 5 we give rigorous estimates of the bias and variance of the estimators $\tilde{R}(t)$ and $\hat{R}(t)$. Such estimates will show that, as t increases, when the algorithm stops, on average at least $(1 - \epsilon)\%$ of the low temperature rate has been found.

5. Analysis

The approximation $\tilde{p}_j(t)$ of $p_j(t)$ is usually considered valid when $\beta^{\mathrm{hi}} \ll V(s_j) - V(m)$, with m the minimizer of V in Ω. To the authors' knowledge, rigorous results are scarce except when $s_j = \mathrm{argmin}_{s_1,\dots,s_N} V(s_j) - V(m)$; see [4] and references therein. However, the following is a consequence of results in [2]:

Theorem 5.1. *Suppose $\Omega = (a, b)$ is an interval and V is a Morse potential. Then for each $t > 0$,*

(5.1) $$\frac{1 - \tilde{p}_j(t)}{1 - p_j(t)} = 1 + O(1/\beta^{\mathrm{hi}}) \text{ as } \beta^{\mathrm{hi}} \to \infty, \qquad j = 1, 2.$$

Proof. An examination of the proof of Theorem 4.1 of [2] shows that for $j = 1, 2$,

$$k_j^{\mathrm{hi}}/\kappa_j = 1 + O(1/\beta^{\mathrm{hi}}) \qquad \text{as } \beta^{\mathrm{hi}} \to \infty,$$

where k_j^{hi} is as in (4.4), and κ_j is as in Theorem 3.2 at temperature $\beta = \beta^{\text{hi}}$. The result follows. $\square$

We next examine the approximation $\hat{p}(t)$ of $p(t)$.

Theorem 5.2. *Conditionally on $N(t) \geq 1$, $\hat{N}_j(t)$ is an unbiased estimator for $\kappa_j t$:*

$$\text{(5.2)} \qquad \mathbb{E}[\hat{N}_j(t) \,|\, N(t) \geq 1] = \kappa_j t.$$

Also conditionally on $N(t) \geq 1$, $\hat{p}_j(t)$ is a conservative estimate of $p_j(t)$:

$$\text{(5.3)} \qquad \mathbb{E}[\hat{p}_j(t) \,|\, N_j(t) \geq 1] \leq p_j(t).$$

Proof. Recall that $N_j(t)$ is a Poisson process with parameter κ_j. Thus,

$$\mathbb{E}[\hat{N}_j(t) \,|\, N_j(t) \geq 1] = \left(1 - e^{-\kappa_j t}\right)^{-1} \sum_{n=2}^{\infty} n \frac{(\kappa_j t)^n e^{-\kappa_j t}}{n!}$$

$$= \frac{\kappa_j t}{1 - e^{-\kappa_j t}} \sum_{n=1}^{\infty} \frac{(\kappa_j t)^n e^{-\kappa_j t}}{n!} = \kappa_j t.$$

Since $x \mapsto 1 - e^{-x}$ is a concave function, the second statement of the theorem follows from Jensen's inequality. $\square$

The reason that we consider conditional expectations in Theorem 5.2 is that Algorithm 2.2 cannot stop before $N(t) \geq 1$. Thus, we want estimates conditioned on that event. We call $\hat{p}_j(t)$ a conservative estimate for $p_j(t)$ because it is a lower bound on average, so that using $\hat{p}_j(t)$ in place of $p_j(t)$ leads to a larger average stopping time for Algorithm 2.2.

Before proceeding we define, for a real-valued random variables X and Y,

$$\text{(5.4)} \qquad \text{Bias}(X, Y) := \mathbb{E}[X - Y], \qquad \text{MSE}(X, Y) := \text{Bias}(X, Y)^2 + \text{Var}(X).$$

Observe that the mean square error is not symmetric in its arguments.

Theorem 5.3. *Write $q_j(t) = 1 - p_j(t) = \exp[-\kappa_j t]$ and $K = k_1 + \ldots + k_N$. For the estimator $\tilde{R}(t)$,*

$$\left| \text{Bias}(\tilde{R}(t), R(t)) \right| \leq N \max_j \left| \text{Bias}(\tilde{p}_j(t), p_j(t)) \right| + \frac{K}{\min_j k_j} \bar{R}(t) \max_j q_j(t),$$

$$\text{(5.5)} \quad \text{Var}(\tilde{R}(t)) \leq 4 \frac{K^2}{\min_j k_j^2} \bar{R}(t)^2 \max_j q_j(t),$$

$$\text{MSE}(\tilde{R}(t), R(t)) \leq 2N^2 \max_j \text{MSE}(\tilde{p}_j(t), p_j(t))$$

$$+ \frac{K^2}{\min_j k_j^2} \left(2 \max_j q_j(t) + 4 \right) \bar{R}(t)^2 \max_j q_j(t).$$

For the estimator $\hat{R}(t)$,

(5.6)

$$\left|\text{Bias}(\hat{R}(t), R(t))\right| \leq N \max_j |\text{Bias}(\hat{p}_j(t), p_j(t))| + \frac{K}{\min_j k_j} \bar{R}(t) \max_j q_j(t),$$

$$\text{Var}(\hat{R}(t)) \leq \frac{2K^2}{\min_j k_j^2} \bar{R}(t)^2 \max_j q_j(t) + \left(1 + 2N^2 \max_j q_j(t)\right) \max_j \text{Var}(\hat{p}_j(t)),$$

$$\text{MSE}(\hat{R}(t), R(t)) \leq \left(1 + N^2 + 2N^2 \max_j q_j(t)\right) \max_j \text{MSE}(\hat{p}_j(t), p_j(t))$$

$$+ \frac{4K^2}{\min_j k_j^2} \bar{R}(t)^2 \left(1 + \max_j q_j(t)\right) \max_j q_j(t).$$

Here, all maxima and minima are taken over $j \in \{1, \ldots, N\}$.

Proof. We give proofs in Section 6 below. □

We note that some of the bounds in Theorem 5.3 have been loosened so that simpler expressions are obtained. This will become clear in the derivation of the bounds in Section 6 below. We highlight that the bias is bounded by the bias of the estimate of $p_j(t)$, together with another term representing an "inherent" bias associated with $\bar{R}(t)$. This second term may be approximated by noting that $|\bar{R}(t)| < 1$ for all t and, due to Theorem 5.1, we expect $q_j(t)$ can be estimated by the known function $\tilde{p}_j(t)$ or $\hat{p}_j(t)$.

6. ESTIMATES

In this section we give a proof of Theorem 5.3. Recall that $q_j(t) := 1 - p_j(t)$ and $K := \sum_{j=1}^N k_j$ is the total reaction rate. For brevity, we will sometimes suppress the t dependence in our expressions. Also, all sums are over $1, \ldots, N$ unless otherwise indicated.

6.1. **Preliminary Calculations.** Observe that

$$\text{Bias}(\tilde{R}(t), R(t)) = \text{Bias}(\tilde{R}(t), \bar{R}(t)), \qquad \text{MSE}(\tilde{R}(t), R(t)) = \text{MSE}(\tilde{R}(t), \bar{R}(t))$$

and similarly for $\hat{R}(t)$; this fact will be used below without comment. There are a few expressions that will show up repeatedly in the analyses of both $\tilde{R}$ and $\hat{R}$. We analyze them here for simplicity. Let

(6.1)
$$\xi_i = k_i + \sum_{m \neq i} k_m \chi_m$$

We make the following calculations:

(6.2a)
$$k_i \leq \xi_i \leq K$$

(6.2b)
$$\mathbb{E}[\xi_i] = k_i + \sum_{m \neq i} p_m k_m = K - \sum_{m \neq i} q_m k_m$$

A lower bound on this can be obtained from Jensen's inequality,

(6.3)
$$\mathbb{E}[\xi_i^{-1}] \geq \mathbb{E}[\xi_i]^{-1} = \frac{1}{K - \sum_{m \neq i} q_m k_m} \geq \frac{1}{K} + \frac{1}{K^2} \sum_{m \neq i} k_m q_m$$

while an upper bound can be obtained from the Edmunson-Madansky inequality,

$$(6.4) \qquad \mathbb{E}[\xi_i^{-1}] \leq \frac{1}{k_i} \frac{K - \mathbb{E}[\xi_i]}{K - k_i} + \frac{1}{K} \frac{\mathbb{E}[\xi_i] - k_i}{K - k_i} = \frac{1}{K} + \frac{1}{k_i K} \sum_{m \neq i} k_m q_m$$

In the same way,

$$(6.5) \qquad \mathbb{E}[\xi_i^{-2}] \geq \mathbb{E}[\xi_i]^{-2} = \frac{1}{\left(K - \sum_{m \neq i} q_m k_m\right)^2} \geq \frac{1}{K^2} + \frac{2}{K^3} \sum_{m \neq i} q_m k_m$$

and

$$(6.6) \qquad \mathbb{E}[\xi_i^{-2}] \leq \frac{1}{k_i^2} \frac{K - \mathbb{E}[\xi_i]}{K - k_i} + \frac{1}{K^2} \frac{\mathbb{E}[\xi_i] - k_i}{K - k_i} = \frac{1}{K^2} + \frac{K + k_i}{k_i^2 K^2} \sum_{m \neq i} q_m k_m$$

Therefore,

$$(6.7) \qquad \mathrm{Var}(\xi_i^{-1}) \leq \left(\frac{K + k_i}{k_i^2 K^2} - \frac{2}{K^3}\right) \sum_{m \neq i} q_m k_m \leq \frac{2}{K k_i^2} \sum_{m \neq i} q_m(t) k_m,$$

where we have lost some of the estimate in the last inequality for the sake of conciseness.

6.2. **Estimates for $\tilde{R}$.** Below it is useful to notice that

$$(6.8) \qquad \tilde{R}(t) = \sum_{i=1}^{N} \frac{\tilde{p}_i(t)\chi_i(t)k_i}{k_i + \sum_{m \neq i} \chi_m(t)k_m} = \sum_i \frac{\tilde{p}_i \chi_i k_i}{\xi_i}.$$

6.2.1. *Bias.* We begin with the direct calculation

$$\begin{aligned}
\mathbb{E}[\tilde{R} - \bar{R}] &= \sum_{i=1}^{N} \mathbb{E}\left[\frac{\chi_i \tilde{p}_i k_i}{\xi_i} - \frac{\chi_i k_i}{K}\right] \\
&= \sum_{i=1}^{N} (\tilde{p}_i - p_i)\mathbb{E}\left[\frac{\chi_i k_i}{\xi_i}\right] + \sum_{i=1}^{N} \mathbb{E}\left[\frac{\chi_i p_i k_i}{\xi_i} - \frac{\chi_i k_i}{K}\right] \\
&= \sum_{i=1}^{N} (\tilde{p}_i - p_i)\mathbb{E}\left[\frac{\chi_i k_i}{\xi_i}\right] + \sum_{i=1}^{N} \underbrace{\mathbb{E}\left[\frac{Kp_i}{\xi_i} - 1\right]}_{\equiv b_i} \frac{p_i k_i}{K}.
\end{aligned}$$

Using (6.3) and (6.4),

$$\frac{1}{K} \sum_{m \neq i} k_m q_m - q_i \leq b_i \leq \frac{1}{k_i} \sum_{m \neq i} k_m q_m - q_i.$$

Thus,

$$\left|\sum_{i=1}^{N} b_i \frac{p_i k_i}{K}\right| \leq \sum_{i=1}^{N} \left(\sum_{j=1}^{N} \frac{k_j}{k_i} q_j\right) \frac{p_i(t)k_i}{K} \leq \frac{K \max_j q_j(t)}{\min_j k_j} \bar{R}(t).$$

Combining the above expressions gives

$$(6.9) \qquad \left|\mathrm{Bias}(\tilde{R}(t), \bar{R}(t))\right| \leq N \max_i |\tilde{p}_i(t) - p_i(t)| + \frac{K \max_i q_i(t)}{\min_i k_i} \bar{R}(t).$$

6.2.2. *Variance.* For the variance, we first write

$$(6.10) \qquad \tilde{R} - \mathbb{E}[\tilde{R}] = \sum_{i=1}^{N} \left(\frac{\chi_i}{\xi_i} - \mathbb{E}\left[\frac{\chi_i}{\xi_i}\right] \right) \tilde{p}_i k_i.$$

Hence,

$$(6.11) \qquad \mathrm{Var}(\tilde{R}(t)) = \sum_{i,j=1}^{N} k_i k_j \tilde{p}_i \tilde{p}_j \underbrace{\mathrm{Cov}\left(\frac{\chi_i}{\xi_i}, \frac{\chi_j}{\xi_j} \right)}_{\equiv v_{ij}}.$$

Since $v_{ij} \leq \sqrt{v_{ii}}\sqrt{v_{jj}}$, it will be sufficient for us to analyze the diagonal terms. By Theorem 3.2, χ_i and ξ_i are independent. Thus

$$(6.12) \qquad v_{ii} = \mathbb{E}[\chi_i]^2 \, \mathrm{Var}(\xi_i^{-1}) + \mathbb{E}[\xi_i^{-1}]^2 \, \mathrm{Var}(\chi_i) + \mathrm{Var}(\xi_i^{-1}) \, \mathrm{Var}(\chi_i).$$

Using (6.6) and (6.7),

$$v_{ii} \leq p_i \, \mathrm{Var}(\xi_i^{-1}) + p_i q_i \mathbb{E}[\xi_i^{-2}]$$

$$(6.13) \qquad \leq p_i \left(\frac{K+k_i}{k_i^2 K^2} - \frac{2}{K^3} \right) \sum_{m \neq i} q_m k_m + p_i q_i \left(\frac{1}{K^2} + \frac{K+k_i}{k_i^2 K^2} \sum_{m \neq i} q_m k_m \right)$$

$$\leq \frac{p_i q_i}{K^2} + \frac{4 p_i}{k_i^2 K} \sum_{m \neq i} q_m k_m \leq \frac{4 p_i}{k_i^2} \max_j q_j \leq \frac{4}{k_i^2} \max_j q_j(t)$$

$$\leq \frac{4}{\min_j k_j^2} \max_j q_j(t).$$

We have made some sacrifices in the last inequalities in order to obtain a more concise expression. Consequently,

$$(6.14) \qquad \begin{aligned} \mathrm{Var}(\tilde{R}(t)) &\leq \sum_{i,j=1}^{N} k_i k_j \tilde{p}_i(t) \tilde{p}_j(t) \sqrt{v_{ii}} \sqrt{v_{jj}} \\ &\leq \frac{4 K^2}{\min_i k_i^2} \bar{R}(t)^2 \max_i q_i(t). \end{aligned}$$

6.2.3. *MSE.* Combining (6.9) and (6.14), we then obtain

$$(6.15) \qquad \begin{aligned} \mathrm{MSE}(\tilde{R}(t), \bar{R}(t)) &\leq 2N^2 \max_i |\tilde{p}_i(t) - p_i(t)|^2 \\ &\quad + \frac{K^2}{\min_i k_i^2} \left(2 \max_i q_i(t) + 4 \right) \bar{R}(t)^2 \max_i q_i(t). \end{aligned}$$

In this calculation, we see that the mean square error may ultimately be dominated by how well the $\tilde{p}_i$ approximate the p_i.

6.3. **Estimates for $\hat{R}$.** We begin by noting that, since $\hat{p}_j(t) = 0$ if $\chi_j(t) \neq 1$,

$$(6.16) \qquad \hat{R}(t) = \sum_j \frac{\hat{p}_j(t) k_j}{k_j + \sum_{m \neq j} \chi_m(t) k_j}.$$

6.3.1. *Bias.* We begin by writing

$$(6.17) \qquad \hat{R} - \bar{R} = \sum_{i=1}^{N} (\hat{p}_i - p_i) \frac{k_i}{\xi_i} + \sum_{i=1}^{N} \frac{k_i p_i}{\xi_i} - \frac{k_i p_i}{K}$$

so that, after taking an expectation,

$$(6.18) \qquad \mathbb{E}[\hat{R} - \bar{R}] = \sum_{i=1}^{N} \mathbb{E}\left[(\hat{p}_i - p_i)\frac{k_i}{\xi_i}\right] + \sum_{i=1}^{N} \left(\mathbb{E}\left[\frac{K}{\xi_i}\right] - 1\right) \frac{k_i p_i}{K}.$$

Hence,

$$(6.19) \qquad \left|\mathrm{Bias}(\hat{R}(t), \bar{R}(t))\right| \leq N \max_i |\mathrm{Bias}(\hat{p}_i(t), p(t))| + \frac{K}{\min_i k_i} \bar{R}(t) \max_i q_i(t),$$

and we see that the observed bias is controlled by the biases of the approximate probabilities, $\hat{p}_i$, and the inherent bias of the Chill type estimators.

6.3.2. *Variance.* For the variance, we have

$$(6.20) \qquad \mathrm{Var}(\hat{R}) = \sum_{i,j=1}^{N} k_i k_j \underbrace{\mathrm{Cov}\left(\frac{\hat{p}_i}{\xi_i}, \frac{\hat{p}_j}{\xi_j}\right)}_{\equiv \hat{v}_{ij}}.$$

As before, we only need to study the diagonal entries, and use Theorem 3.2 to obtain

$$
\begin{aligned}
\hat{v}_{ii} &= \mathbb{E}[\hat{p}_i]^2 \mathrm{Var}(\xi_i^{-1}) + \mathbb{E}[\xi_i^{-1}]^2 \mathrm{Var}(\hat{p}_i) + \mathrm{Var}(\hat{p}_i)\mathrm{Var}(\xi_i^{-1}) \\
&\leq \mathrm{Var}(\xi_i^{-1}) + \mathbb{E}[\xi_i^{-2}]\mathrm{Var}(\hat{p}_i) \\
(6.21) \qquad &\leq \frac{2}{\min_i k_i^2} \max_i q_i + \left(\frac{1}{K^2} + \frac{2}{\min_i k_i^2} \max_i q_i\right) \mathrm{Var}(\hat{p}_i) \\
&\leq \frac{2}{\min_i k_i^2} \max_i q_i + \left(\frac{1}{K^2} + \frac{2}{\min_i k_i^2} \max_i q_i\right) \max_i \mathrm{Var}(\hat{p}_i).
\end{aligned}
$$

We note that these estimates require full independence of $N_j(t)$ for $j = 1, \ldots, N$, not just independence of the $\chi_j(t)$. Now,

$$(6.22) \quad \mathrm{Var}(\hat{R}(t)) \leq \frac{2K^2}{\min_i k_i^2} \bar{R}(t)^2 \max_i q_i(t) + \left(1 + 2N^2 \max_i q_i(t)\right) \max_i \mathrm{Var}(\hat{p}_i(t)).$$

6.3.3. *MSE.* We can therefore express the mean square error of estimator $\hat{R}$ as

$$
\begin{aligned}
(6.23) \qquad \mathrm{MSE}(\hat{R}(t), \bar{R}(t)) &\leq \frac{4K^2}{\min_i k_i^2} \bar{R}(t)^2 \left(1 + \max_i q_i(t)\right) \max_i q_i(t) \\
&\quad + \left(1 + N^2 + 2N^2 \max_i q_i(t)\right) \max_i \mathrm{MSE}(\hat{p}_i(t), p_i(t)).
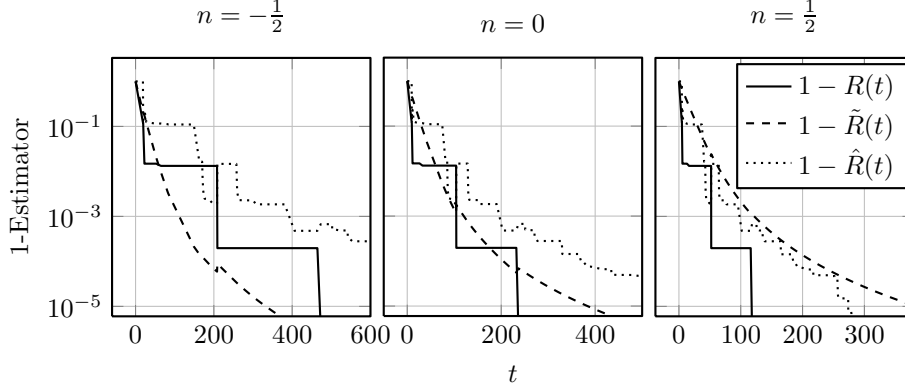\end{aligned}
$$

FIGURE 1. Comparison of the Chill type estimators $\tilde{R}(t)$ and $\hat{R}(t)$ to the true expected proportion of the low temperature rate found, $R(t)$, on a test system that can deviate from the Erying-Kramers law.
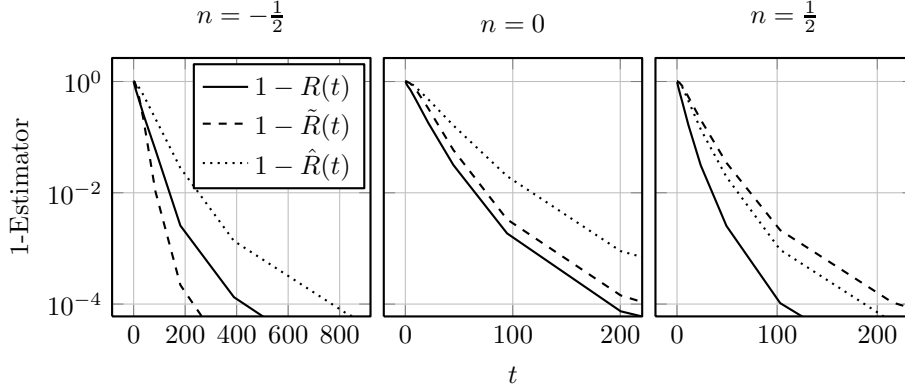

FIGURE 2. Comparison of the expected value of the Chill type estimators $\tilde{R}(t)$ and $\hat{R}(t)$ to the true expected proportion of the low temperature rate found, $R(t)$, on a test system that can deviate from the Erying-Kramers law.

7. DISCUSSION

We have considered three Chill type estimators and shown them to be consistent. Their biases are small, relative to their variances, and thus we have good estimators of $R(t)$, the true fraction of the observed rate in the system. They represent a significant improvement over the original AKMC stopping criterion presented in [17]. Indeed, these prior approaches attempted to estimate the fraction of the saddles observed when, in fact, it is the fraction of the observed rate that is of fundamental importance.

As an example, we will compare the accuracy of both estimators using a test system that consists of saddle points s_j corresponding to potential energy barriers $V(s_j) - V(m) = 1 + \frac{4}{19}j$, for $j = 0, \ldots, 19$. The test system has rates that obey a

modified Arrhenius equation with the form:

$$(7.1) \qquad \tilde{k}_j^{\text{hi}} = \left(\frac{\beta^{\text{lo}}}{\beta^{\text{hi}}}\right)^n g_j \exp[\beta V(s_j) - V(m)].$$

Compare to equation (1.1) (recall the subscript i has been suppressed). The variable n controls how the rates deviate from an unmodified Arrhenius rate law. When $n = 0$ the modified rates $\tilde{k}_j^{\text{hi}}$ are equal to the unmodified rates k_j^{hi}, while when $\beta^{\text{hi}} < \beta^{\text{lo}}$, the modified rates are larger (resp. smaller) than the unmodified rates if $n > 0$ (resp. $n < 0$).

We use Algorithm 2.2 on the test system with modified rates $\tilde{k}_j^{\text{hi}}$. This means $(N_j(t))_{0 \le t \le t_{\text{sim}}}^{j=1,\ldots,N}$ are independent Poisson processes with parameters $\tilde{k}_j^{\text{hi}}$. To compute $R(t)$, we use (4.1) and sample $\chi_j(t)$ via (2.2). To compute $\tilde{R}(t)$ we use the unmodified Arrenius rates k_j^{hi} in equation (4.4). For each of $R(t)$, $\tilde{R}(t)$ and $\hat{R}(t)$, the low temperature rates $k_j = k_j^{\text{lo}}$ used in equations (4.1) and (4.5) are the same. We take $g_j = 1$ for all j and $\beta^{\text{hi}} = 2.5$, $\beta^{\text{lo}} = 10.0$. The variable n was varied to compare the cases where the Erying-Kramers rates k_j^{hi} underestimate ($n = \frac{1}{2}$), overestimate ($n = -\frac{1}{2}$), and provide an exact estimate ($n = 0$) of the modified rates $\tilde{k}_j^{\text{hi}}$. Results are shown in Figures 1 and 2. The test system shows that $\tilde{R}(t)$ can overestimate $R(t)$ if the Eyring-Kramers rate deviates from the true rate at β^{hi}, while $\hat{R}(t)$ tends to provide a conservative estimate of $R(t)$.

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